

Tumors of the Thyroid and Parathyroid Glands

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SINCE THE PRINCIPAL emphasis of the California Cancer Commission series has been upon malignant tumors, the present article will be particularly concerned with tumors of the thyroid rather than those of the parathyroid glands. The series from the University of California Medical Center on which this report is based includes more than 400 malignant tumors of the thyroid gland but no authentic instances of malignant disease of the parathyroid were found in more than 140 cases of hyperparathyroidism.

Although the first report on the relationship of radioactive iodine to cancer of the thyroid gland from the University of California Medical Center was published in 1940,¹⁷ no mention was made of I¹³¹ by the senior author in his earlier article for *Cancer Studies* published in 1948. With the introduction of radioactive iodine much has been learned about the diagnosis and treatment of thyroid cancer, but it has not proved to be the answer to therapy hoped for in the early days of its use. As is true with cancer in other regions, early diagnosis and complete surgical removal of malignant lesions of the thyroid gland offer the best prognosis. The differences of opinion regarding cancer of the thyroid gland center around the incidence, diagnosis and prognosis, extent of operation and the advisability and amount of internal or external irradiation.

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Carcinoma of the Thyroid Gland

Clinical Diagnosis. Goiters become surgical problems for the following reasons: (1) hyperthyroidism, (2) mechanical difficulties, and (3) the question of malignancy. The diagnosis and treatment of hyperthyroidism will not be considered here except to point out that the actual presence of hyperthyroidism does not rule out malignant disease, but only upon very rare occasions is it encountered in diffuse toxic, or even nodular toxic, goiter. Displacement of and pressure upon the cervical and mediastinal structures may accompany either benign or malignant enlargement of the thyroid gland and these cases become surgical problems because of associated symptoms. The number of patients being treated surgically because of pressure symptoms has not varied greatly over the years but the number of patients upon whom operation is performed for treatment of hyperthyroidism has declined steadily as medical management has become more effective. However, the percentage of patients operated upon because of possible malignant change is increasing in all series reported.^{16,38}

It is generally agreed that most malignant lesions of the thyroid gland first appear as nodular goiters. The diagnostic problem is one of determining which nodular goiters are benign and which should be suspected of harboring malignant changes. Certain findings in the history and physical examination should put nodular goiters under suspicion. The first and most important is recent, rapid growth of the gland or nodule. If the patient is to be under

observation or treatment, caliper measurements of the gland and the nodules should be made to determine growth or regression. Hoarseness and dysphagia suggest malignant change but are occasionally seen in thyroiditis. In the latter case the gland may be somewhat tender, is usually firm and of normal configuration. On the scintigram, thyroiditis is usually manifested by a meager, uniform uptake of radioactive iodine rather than "cold" areas. If hoarseness is found to be due to vocal cord paralysis, this points more strongly to malignant disease.

Diagnosis

Single Nodule. The value of classifying glands as single or multinodular is often discussed. The accuracy of clinical evaluation of the single nodule is in question, and varies from 100 per cent, as reported by Slater and Lipton,³³ to 50 per cent as reported by Boggs.⁶ In our series at the University of California Medical Center, San Francisco, operative and pathological findings confirmed the presence of a single nodule 162 times in 192 cases in which it was so diagnosed preoperatively.²⁰ Williams and coworkers³⁹ showed that the likelihood of malignant change in a goiter with a clinically solitary nodule is three to four times greater than if the goiter is multinodular. They found that 14.6 per cent of uninodular goiters were malignant compared with 4.3 per cent of multinodular glands. Shimaoka and his coworkers³¹ found no significant difference in the frequency of malignant change between uninodular and multinodular goiter. Bartels³ stated that in the diagnosis of carcinoma of the thyroid, the clinical history, examination of the gland, and even the surgeon's opinion at the time of operation are often inaccurate.

Scintiscan. A scintiscan obtained after the ingestion of a test dose of I^{131} may be useful in detecting malignant change in a nodular goiter. The finding of a "cold" nodule by this method is consistent with but not diagnostic of cancer. Dobyns¹⁴ experience over the past 15 years has shown no hyperfunctioning nodules that contained carcinoma, and he has pointed out that even the most actively functioning carcinomas of the thyroid take up I^{131} to a lesser degree than does normal thyroid tissue. He stated that the appraisal of functional quality of the irregular areas in a nodular goiter should be regarded as obligatory before surgical treatment is undertaken. It was his opinion that all carcinomas would be found among the so-called "cold nodules." Meadows²⁵ has found carcinoma in 58 per cent of nonfunctional, clinically solitary nodules. Becker and his colleagues⁴ reported two cases of carcinoma in "hot" nodules.

Therapeutic Test. Another diagnostic method favored by some investigators is a therapeutic test

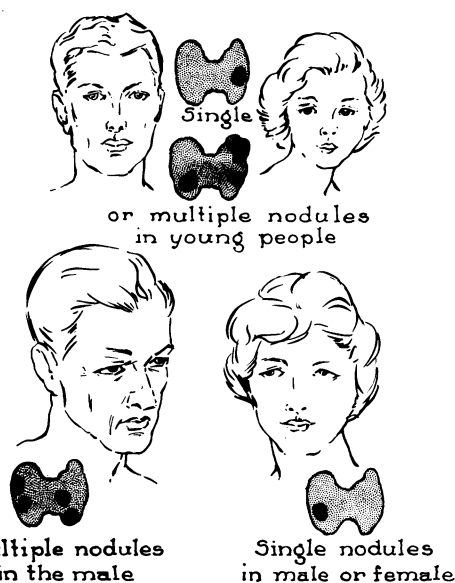


Figure 1.—Types of patient in whom malignant goiter should be suspected when nodular goiter is present.

based on the assumption that nodular goiters occur because of oversecretion of thyroid-stimulating hormone (TSH). This test is designed to block the stimulation of TSH by administration of sufficient amounts of desiccated thyroid, I-triiodothyronine (T_3), or sodium levothyroxine (T_4). Some investigators, notably Astwood and his colleagues,¹ strongly endorse this test and feel that only the nodular goiters that do not disappear after thyroid administration should be treated surgically. Others, including Byrd and coworkers⁹ and Colcock and Cattell,³¹ feel that thyroid administration may mask the clinical picture and lead to a fatal delay in the diagnosis of malignant disease.

Bowens and coworkers⁷ suggest that little risk is involved in administering thyroid or T_3 to patients with asymptomatic thyroid nodules if there are no clinical indications of cancer. Shimaoka and his colleagues³¹ are of the same opinion. If little reduction in the size of the thyroid occurs after this test administration of hormones or if the size increases, as demonstrated by caliper measurements during the test, then surgical exploration becomes imperative. It is our opinion that the administration of thyroid or the faster-acting T_3 as a test for malignant change should be limited to not more than five months. Badillo and coworkers² suggest that six months may be too long a therapeutic test. We warn against indiscriminate or prolonged unresponsive use of hormone therapy in nodular goiter. Disappearance of nodules is relatively rare and a slight decrease in the size of the gland or nodules does not rule out malignant change. Vieth and coworkers⁴⁷ recommended only two to four

months of suppression therapy before operation and emphasized the importance of hormone therapy after operation for either benign or malignant goiter.

Statistical Suspicion. In certain patients suspicion is aroused by the presence of a nodular goiter or persistent cervical adenopathy.^{22,38} These patients include: (1) prepubertal children, (2) men with non-toxic nodular goiter, and (3) any patient with a solitary nodule (Figure 1). In children and adult males such findings are suspicious since these groups have not been exposed (as adult women are) to the stimulus of the varying physiologic demands for thyroid activity associated with menstruation, childbearing, lactation and the climacteric. Hayles and his coworkers¹⁸ have agreed that malignant disease of the thyroid should be suspected in any child with nodular goiter or persistent cervical adenopathy until proved not to be present.

One of us (RW) found carcinoma in five out of 30 (16.6 per cent) male patients operated upon for nontoxic nodular goiter. Majarakis and his coworkers²³ found malignant change four times as often in males with non-toxic nodular goiters as in females. The solitary nodule is suspect in women because such nodules are more often neoplastic than are the involuntary nodules involved in multinodular goiter.

Because the only way to determine malignancy positively is by microscopic examination and since the choice of proper therapy depends upon the type of malignant change, a review of the histologic types of malignant lesions and their life histories is in order.

General Pathology

The two basic forms of thyroid carcinoma are papillary and follicular. Some papillary carcinomas contain only a few papillary structures and may display mainly follicular or solid lobular patterns. The recognition of the true papillary nature of neoplasms that have a follicular pattern is important because of the significant differences in the clinical course and accepted methods of therapy of the two neoplasms.

Papillary Carcinoma. Papillary carcinoma is the most common form of thyroid cancer in the United States. It occurs at all ages but is most frequent in persons between the ages of 20 and 40. It is usually a slowly growing neoplasm which tends to invade and permeate the lymphatic channels of the thyroid and thus extend to the opposite lobe. It also invades blood vessels and metastasizes to distant sites where it may remain dormant for many years. More commonly, metastasis appears first in

pericapsular lymph nodes and then in regional lymph nodes in the cervical chain.

Follicular Carcinoma. Several forms of follicular carcinoma are encountered. Localized follicular carcinoma presents as a nodule differing from a benign adenoma by the presence of capsular or vascular invasion, or both; and some degree of cellular and nuclear pleomorphism and mitotic activity. Histologic patterns are predominantly microfollicular and trabecular. The nuclei are unlike those of papillary carcinoma; they are smaller and contain abundant, coarse chromatin material. These follicular carcinomas rarely invade lymphatic channels, but distant metastasis, usually in the skeleton, results from intravascular growth and extension of the neoplasm. Localized follicular carcinoma occurs at all ages, except during the first nine years of life.

Invasive follicular carcinoma may originate from a pre-existing benign adenoma, and an encapsulated angio-invasive adenoma or localized follicular carcinoma may be one stage of its development. These neoplasms spread in the thyroid gland by local invasion rather than lymphatic permeation. Varying degrees of follicular differentiation and colloid formation are usually present. The nuclei are dense and hyperchromatic as in localized follicular carcinoma. The peak incidence of invasive follicular carcinoma occurs in patients between the ages of 50 and 59. The frequency of distant metastasis resulting from vascular dissemination is considerably greater in follicular carcinoma than in papillary carcinoma.

Included in the group of follicular carcinomas are medullary or solid carcinomas, described by Hazard and coworkers.¹⁹ The neoplasms are characterized by a relatively solid epithelial pattern although a few microfollicles are frequently observed. Abundant deposits of amyloid are invariably found in the stroma of the supporting connective tissue of these neoplasms and there is evidence that the amyloid is produced by the neoplastic epithelium. Unlike other follicular carcinomas, these lesions have a propensity for metastasizing to regional lymph nodes. Distant metastasis also occurs in almost half the cases. Medullary carcinomas are found in patients between the ages of 28 and 80, with the highest incidence between 50 and 59.

Anaplastic Carcinoma. Anaplastic carcinoma is an undifferentiated form of thyroidal epithelial neoplasm that shows no papillary and little or no follicular formation. These neoplasms, which occur almost exclusively in women, grow extremely rapidly and most of the patients die within a few months. It is believed that some anaplastic or undifferentiated carcinomas may originate from either papillary or follicular carcinomas and that

they represent the undifferentiated end-stage of differentiated thyroid carcinomas. Most patients with anaplastic carcinoma have had goiter for many years but a superimposed, rapidly growing malignant neoplasm usually does not appear until after the age of 40 or 50. The predominant microscopic pattern in most cases consists of large sheets of extremely bizarre, large, multinucleated or elongated spindle-shaped cells. Some of these giant-cell carcinomas may have an epidermoid component. However, patients with other anaplastic carcinomas which consist of large or small cells, including spindle-cell variants, may survive longer than patients with giant-cell anaplastic carcinoma. Anaplastic carcinoma frequently invades the cervical tissues beyond the capsule of the thyroid, and metastasis to regional lymph nodes and distant sites is common. As a rule, however, the extremely rapid growth causes death from respiratory obstruction before distant metastasis becomes clinically evident.

Pathologic Diagnosis. After surgical removal, the thyroid specimen should be submitted to the pathologist for examination. The external surface of the tissue may reveal evidence of malignant neoplasia in the form of a thickened, scarred and retracted thyroid capsule, enlarged pericapsular lymph nodes or enlarged vessels invaded by neoplastic tissue. When the thyroid specimen, usually a lobe, is sectioned, gross characteristics of the tissue may suggest whether an existing nodule is benign or malignant; for example, benign nodules are almost always well-encapsulated. Extensions of the tissue comprising a nodule beyond the capsule of the nodule suggest invasive tendencies, and satellite nodules outside the capsule of the nodule are further evidence of malignancy. Follicular or trabecular adenomas generally have a yellowish-pink, yellowish-tan, or pinkish-tan uniform, homogeneous, bulging surface, but papillary neoplasms, whether benign or malignant, have a characteristically granular and pebbly cut surface. Medullary carcinoma appears firm, pale and opaque due to its amyloid content, and central calcification is frequent. Anaplastic carcinoma as a rule is meaty, vascular, and often hemorrhagic and partially necrotic. In contrast, benign macrofollicular adenomas (so-called involutionary nodules) are circumscribed and encapsulated. The variegated cut surface has an abundance of glistening colloid, and almost always shows signs of old and recent hemorrhage, fibrosis and deposits of cholesterol.

Although gross examination of the tissue may lead to an accurate diagnosis, examination by frozen section should also be done. Tissue blocks to be examined should be selected from character-

istic portions of the nodule. In the case of a partially encapsulated nodule, sections at points where the capsule appears deficient may reveal neoplastic invasion of adjacent thyroid parenchyma or blood vessels. Frozen sections of thyroid tissue are notoriously difficult to prepare since the tissue tends to fold and wrinkle, and colloid from follicles may become displaced. The increasing use of the cryostat in place of the freezing microtome solves this problem, since sections prepared with this apparatus are almost as good as those made from paraffin blocks. In some cases, thyroid neoplasms may be so well-differentiated that they closely resemble normal thyroid tissue, although the lobular pattern of normal thyroid tissue is not present.

Many papillary carcinomas have a predominantly follicular pattern. Differentiation from follicular carcinoma usually depends upon demonstrating the characteristically pale, opaque, poorly-staining nuclei of papillary carcinoma. However, these nuclei stain with thionine, frequently used to stain frozen sections, which may lead to an incorrect diagnosis of follicular carcinoma. For that reason, frozen sections of thyroid tissue should be stained with hematoxylin and eosin. Papillary carcinomas may also be identified by the presence of typical concentric calcific structures or psammoma bodies. Primary papillary carcinomas frequently contain a central zone of scarring with calcific deposits. Intraglandular extensions of papillary carcinomas do not as a rule show these changes. If a papillary neoplasm is free of such complications, a search for primary papillary carcinoma in the opposite lobe should be made.

The preparation of permanent paraffin sections should include multiple blocks from the periphery of circumscribed or encapsulated nodules in order to demonstrate intravascular invasion. A careful search should be made in the thyroid capsule for adherent pericapsular lymph nodes, and multiple sections of the uninvolved portions of the gland should be examined for evidence of intraglandular extension.

Treatment

Although it is agreed that surgical removal is the most effective treatment of cancer of the thyroid, controversy still centers around the indications for biopsy, lobectomy, total thyroidectomy and the combination of these with modified or radical neck dissection.

Incisional Biopsy. When a differential diagnosis must be made between infiltrating carcinoma and thyroiditis, an incisional biopsy is occasionally warranted. If the presence of thyroiditis is confirmed, it is best handled by means other than surgical removal. If infiltrating carcinoma is found,

the biopsy site can be excised with the radical excision of carcinoma, the type of which is determined by the biopsy findings. Needle biopsy is not used at the University of California Medical Center; it can be relied upon only for the detection of thyroiditis in questionable cases and cannot be trusted to rule out malignant change.

Excisional Biopsy. Only when there is the problem of a differential diagnosis between lymphoma and metastatic carcinoma in a young person is excisional biopsy of a node justified. If excisional biopsy reveals thyroid carcinoma metastatic to a lateral lymph node, an intelligent and effective operation based on the microscopic diagnosis can be planned to include excision of the biopsy site.

Lobectomy. Probably the most common and satisfactory approach to microscopic diagnosis is excisional biopsy and lobectomy. The shelling out of a suspicious or solitary nodule should be condemned. If unsuspected follicular carcinoma is found in paraffin sections after a lobectomy with adequate margins, we do not advise immediate further operation. However, if lobectomy reveals papillary carcinoma or if signs of multicentricity or intraglandular lymphatic spread are present, immediate total thyroidectomy is recommended. Statistics from the University of California Medical Center show little difference in the number and severity of complications following total and subtotal thyroidectomy for carcinoma³⁰ except for the greater incidence of hypoparathyroidism in the former.

Total Thyroidectomy. The main hazards in total thyroidectomy are bilateral damage to the recurrent laryngeal nerves and persistent postoperative parathyroid insufficiency. Recurrent laryngeal nerves can usually be preserved by adequate exposure and careful dissection unless they are actually involved in the malignant process. Preservation of parathyroid function is more difficult. When feasible, it is desirable to leave a small portion of the posterior capsule of the uninvolved thyroid lobe, thereby preserving the blood supply and integrity of at least one parathyroid gland.

The advocates of total thyroidectomy for all cases of cancer of the thyroid^{11,12,28,29} have recommended this procedure in preference to unilateral lobectomy, since 35 per cent of the group treated by unilateral lobectomy have had recurrence in the contralateral lobe. Tollefsen and DeCosse,³⁶ after finding a recurrence rate of 3.7 per cent in the contralateral lobe, stated that total thyroidectomy for papillary carcinoma of the thyroid is unjustified. They reached this conclusion in spite of the fact that microscopic carcinoma was found in the contralateral lobe of 30 per cent of their patients in whom a total thyroidectomy was performed as initial

surgical treatment. MacDonald and Kotin,⁷¹ early advocates of total thyroidectomy for papillary carcinoma, believe that total lobectomy is too drastic in benign goiter and is inadequate for malignant tumors. They consider total thyroidectomy and regional dissection mandatory for established cases of papillary carcinoma and state that radical neck dissection should be limited to the side where positive node metastasis has been demonstrated.

We believe that no rules can be laid down as to the extent of operation, and that the decision to perform total thyroidectomy with or without radical neck dissection depends upon the pathological findings on frozen sections, age of the patient, degree of involvement, presence of demonstrable adenopathy and the risk involved.

Radical Neck Dissection. More controversy probably exists concerning neck dissection than any other form of surgical treatment of cancer of the thyroid. We completely agree with Thomas,³⁴ and Macdonald and Kotin²¹ who feel that neck dissection in thyroid cancer is indicated in the presence of enlarged involved nodes. Thomas³⁴ points out that carcinoma of the thyroid is unique in that the routes of lymphatic drainage are singularly available for examination at the time of removal of the primary tumor. The surgeon familiar with these common routes should be able to detect palpable enlarged nodes and to have them examined cryostatally for malignant change at the time of operation. We concur with Thomas³⁴ and Dobyns¹⁴ that the type of radical neck dissection performed for malignant lesions of the lip, tongue, mouth and pharynx is seldom necessary to eliminate carcinoma of the thyroid except in the infrequent instances in which it has spread to the anterior superior cervical lymph nodes. Dobyns points out that the sternocleidomastoid muscle becomes involved only when other lymphatic pathways are thoroughly blocked by metastatic spread.

By using the criteria laid down by these authors a decision can be made as to the advisability and extent of neck dissection, thus eliminating the questionable value of "prophylactic" dissection and its claimed benefits.

External Radiation Therapy. Papillary adenocarcinomas are only moderately sensitive to irradiation and are rarely, if ever, curable with doses tolerated by normal tissues. These lesions may, however, significantly regress with radiation therapy and thus can be controlled for many years. Radiation therapy is useful when carcinoma is not completely resectable or when local recurrence is inoperable. For papillary adenocarcinoma, the radiation fields should be limited to the area of suspected disease and the doses should be relatively high. Prophy-

lactic irradiation of uninvolved lymph node chains is contraindicated.

Follicular adenocarcinoma is probably less radiosensitive than papillary adenocarcinoma but occasionally it can be controlled for years by aggressive radiation therapy. Neither the thyroid area nor the adjacent lymph nodes should be irradiated prophylactically when surgical removal of diseased tissue is thought to be complete. Radiation therapy for palliation of distant metastatic lesions from papillary or follicular adenocarcinoma is often of value. Local symptoms or tumor growth may be controlled for prolonged periods.

Lymphosarcoma and anaplastic carcinoma often have a pronounced radiosensitivity. These lesions are locally invasive and widely metastatic, characteristics that frequently limit the surgical procedure to biopsy. Local control may be achieved by irradiation, but the prognosis is unfavorable because of the tendency to extensive metastasis. The prognosis for lymphosarcoma arising in the thyroid is more favorable than that for anaplastic carcinoma. Giant-cell anaplastic carcinoma responds poorly to irradiation and is rarely controlled by any means.

Internal Radiation Therapy. The use of I^{131} in the treatment of thyroid cancer is based on the fact that certain of these neoplasms metabolize and concentrate iodine. Thus, I^{131} provides a means of selective internal irradiation. Although a correlation between histologic findings and iodine concentration exists, exceptions are numerous and each patient requires individual study.

In the presence of normal thyroid tissue, thyroid carcinoma rarely shows a significant avidity for radioactive iodine; therefore, in evaluating the possibility of I^{131} therapy, the initial step is complete thyroid ablation by operation, radioactive iodine or both. The subsequent increase in endogenous thyroid-stimulating hormone (TSH) may stimulate the thyroid carcinoma and promote adequate iodine localization in the tumor. Stimulation by exogenous TSH is occasionally successful in patients in whom thyroidectomy has not been performed, but it must be administered each time the patient is to be studied or treated. Exogenous TSH to supplement TSH induced endogenously by thyroidectomy has been used, but it usually has little effect over and above that resulting from thyroid ablation alone. Anti-thyroid drugs have also been used in an attempt to stimulate thyroid carcinoma and thereby increase the uptake of I^{131} . When the blocking action of these drugs is abruptly terminated, stimulation appears as a rebound phenomenon. Thiouracil and its derivatives have been used for this purpose but must be given in large doses for several months. The antithyroid drugs have a theoretical advantage in

that they not only suppress any remnant of non-neoplastic thyroid tissue but also suppress hormone production from the carcinoma itself and thus allow maximal endogenous TSH production. Generally, however, the use of antithyroid drugs has been disappointing.

Data regarding the frequency with which a useful concentration of I^{131} can be activated in thyroid carcinomas vary with the enthusiasm of the investigator. Iodine avidity sufficient to merit consideration of I^{131} therapy can probably be established in about half of all patients with differentiated thyroid carcinoma. Therapy consists of the administration of I^{131} , either in a single dose of 200 or more millicuries, or in several doses at intervals of one to two months. The tumor may regress in from one-third to one-half of the patients so treated, and occasionally evidence of carcinoma will disappear entirely. Since the lesions that respond are usually the untreated, long-standing, well-differentiated follicular and papillary carcinomas, not enough time has elapsed for us to say with certainty that any patient has been cured by I^{131} therapy. Many patients, however, are free of the disease five and ten years after I^{131} treatment and the usefulness of the method in the selected patient is well established.

It should be pointed out that the large amounts of I^{131} required to treat thyroid cancer may have an adverse effect on the hematopoietic system. Depression of this system is usually indicated by a transient reduction of all formed elements of the blood, although fatal depressions in bone marrow have occasionally occurred after massive doses of I^{131} . It has been estimated that total body irradiation from several hundred millicuries of I^{131} will cause leukemia in from three to five per cent of the treated patients.^{8,24} This represents a relatively small risk for the patient with advancing, uncontrolled carcinoma but it certainly rules out the use of I^{131} as prophylactic therapy.

Hormone Therapy. In 1937 Sir Thomas Dunhill¹⁵ described complete regression of the neoplasm in two children with carcinoma of the thyroid after administration of fairly large doses of desiccated thyroid. It has since been found that many of the papillary and alveolar carcinomas of the thyroid are dependent upon stimulation by pituitary thyrotrophin (TSH). It has further been shown that administration of desiccated thyroid, thyroxin, I-triiodothyronine (T_3) or sodium-I-thyroxin (T_4) will inhibit TSH production.³⁵ The conclusion has therefore been reached that the administration of desiccated thyroid, or better, T_3 or T_4 , is indicated postoperatively in the hope that the tumor will become or remain hormone-dependent. In many cases reported in the literature advanced carcinomas have remained hormone-dependent for years.³⁷

Hormone-suppressive therapy should be pushed to tolerance and if T_3 is used, 100 to 200 micrograms daily may be indicated.³⁴

Carcinoma of the Parathyroid Glands

Carcinoma of the parathyroid glands is rare, and is the cause of hyperparathyroidism in only 1 to 3 per cent of all cases.^{5,27} In more than 140 patients with proved hyperparathyroidism, we have not encountered a single instance of carcinoma. That nonfunctioning carcinoma of this gland may exist, as reported by Sieracki and Horn,³² cannot be denied, but because of its microscopic resemblance to carcinoma of the thyroid and other tumors the absence of endocrinological effects throws some suspicion on the diagnosis. One such patient was encountered during this same period.

Clinical, laboratory and roentgenologic evidence of hyperparathyroidism in a patient with a palpable cervical mass, a tumor infiltrating local structures, metastasis to the regional and mediastinal lymph nodes and possibly to the lungs and liver, are among the manifestations of this neoplasm.^{10,26} The diagnosis should be suspected at the operating table when a tumor found near the parathyroid glands is hard, with or without calcification, adherent or infiltrating, and appears malignant on microscopic examination with or without evidence of invasion.¹⁰ Each recurrence of the tumor is accompanied by hormonal manifestations of hyperparathyroidism.

Since this tumor has a tendency to recur locally, attempts should be made to excise it in its entirety, together with removal of involved regional lymph nodes. Some patients survive for several years but eventually succumb from the effects of local recurrence, metastasis, or more commonly from renal insufficiency or hypertension accompanying hyperparathyroidism. If the tumor is still limited to the parathyroid structures when operated upon, total and complete removal of the tumor alone may suffice. In the cases described here, the initial operation was not radical so that recurrence was the rule. Therefore an attempt should be made initially to remove all the tumor, including the thyroid lobe, regional lymph nodes, recurrent nerve and any other structure which is to be sacrificed. Usually, carcinoma has spread beyond the capsule of the gland by the time the diagnosis is made.

Summary

In the early diagnosis and proper treatment of cancer of the thyroid gland the best results are to be expected when a careful preoperative selection is made of patients with nodular goiter who are most liable to harbor malignant change. Any of the following should arouse suspicion: (1) recent growth,

(2) solitary nodules, (3) nodular goiter in children, (4) "cold" nodules, (5) nodular non-toxic goiter in men, (6) lack of regression after hormone administration and (7) vocal cord paralysis.

Proper treatment consists of total surgical extirpation of the primary carcinoma and local metastatic lesions. The decision about the extent of thyroidectomy and glandular dissection should be made on an individual basis at the time of the original operation. By the use of cryostatic sections an immediate diagnosis can usually be made to guide the surgeon to the proper decision in each case.

At times when complete removal is not possible or there are distant metastatic lesions, internal or external radiation is often of benefit. In all cases, especially in younger patients, suppression therapy should be used postoperatively.

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